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09/831,019	07/17/2001	Francois Lang	1721-27	8857

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Nixon & Vanderhye
8th Floor
1100 North Glebe Road
Arlington, VA 22201-4714

EXAMINER

CHEU, CHANGHWA J

ART UNIT	PAPER NUMBER
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1641

DATE MAILED: 07/28/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/831,019

Applicant(s)

LANG ET AL.

Examiner

Jacob Cheu

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 November 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-13 is/are pending in the application.
- 4a) Of the above claim(s) 11-13 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) 1-10 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

DETAILED ACTION

Election/Restrictions

1. Applicants' provisional election of Group I, claims 1-10, with traverse is acknowledged. (Paper # 7, filed 11/26/2002). Applicant objects on the ground(s) that the examiner has not shown that a serious burden would be required to examine all of the claims. This argument has been fully considered, but is not found convincing. Because these inventions are distinct and have acquired separate status in the art as shown by their different classification, recognized divergent subject matter and because the search required for each invention is not substantially coextensive with the search required for the remaining invention, restriction for examination purposes as indicated is proper.

The Restriction Requirement is still deemed proper and is therefore made **FINAL**.

Claim Rejections - 35 USC § 101 and §112, second paragraph

1. Claims 8 and 9 provide for the use of the recited multimers, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claims 8 and 9 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

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pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Scope of enablement

Claims 1-10 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the peptide-specific CD8, does not reasonably provide enablement for *any* structurally different *analogues*. (See Figures 4 and 5) The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention protein analogues commensurate in scope with these claims.

Applicant has not shown that proteins which have been modified are capable of functioning as that which is being disclosed. One skilled in the art had recognized that the term "analogues" encompasses a variety of definitions, i.e. chemical modification, deletions, truncations, substitutions conjugation etc.. The specification only provides the example of substitution of alanine to valine by site mutagenesis. (See page 10, line 8-12) None of the other possible modifications, such as deletions, truncations, or conjugations, have been shown to function as the recited function. Applicant has not shown the enablement of all types of modified proteins as recited in claim 1.

Enablement

Claim 5 is rejected under 35 U.S.C. 112, first paragraph, contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is well-known that protein-protein interaction is a delicate and complicated phenomenon. Applicant has shown that merely change of one amino acid, i.e. from

alanine to valanine, results in substantial reduction of binding affinity on the $\alpha 3$ domain of the heavy chain to the CD8. (See page 10, line 8-12; example 1-3) Although applicant discloses that the modification could be "deletion of at least one amino acid." (See page 5, line 21), it is still speculative that how one skilled in the art could follow without undue burden of research. Most importantly, the instant invention does not provide any example to show (1) where the location of the deletion(s), e.g. what amino acid positions on the protein; (2) how many deletion, or truncation on the target protein, may produce the similar results, i.e. reduced binding, as disclosed in this application. It is possible that deletion may not result in a reduction of the binding, rather it may produce increased affinity of binding due to changes of tertiary structure of the proteins. Since the interaction of protein-protein is unpredictable, and depends on several factors, e.g. tertiary structure, folding, unfolding or thermodynamics of the proteins, this would impose undue experimentation burden to one of ordinary skill in the art to conduct numerous tests to confirm the recited claim.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.
2. Claims 1-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

With respect to claim 1, line 1, "Multimers built up from recombinant proteins analogues" is vague and indefinite. It is unclear what applicant intends to claim, either multimers or protein analogues since the claim language directs to the limitation of the proteins rather than the multimers. Similarly, claims 2-10 share the same problem as in claim 1.

With respect to claim 1, line 1 “built up” is vague and indefinite. It is unclear what applicant means “built up.”

With respect to claim 1, line 3, “modification” is vague and indefinite. It is unclear what applicant means “modification” in the claim, e.g. substitution, truncation, or chemically alteration. Similarly, claim 2-5 share the same problem as claim 1.

With respect to claim 1, line 3, “zone of interaction of a heavy chain with the CD8 co-receptor of T lymphocytes” is vague and indefinite. It is unclear what constitutes the “zone”. Applicant needs to provide a clear metes and bounds, e.g. SEQ ID, for clarification.

With respect to claim 1, line 5, “reduction, or even suppression” is vague and confusing. It is unclear how one skilled in the art to distinguish the “reduction” from “suppression” with respect to the binding affinity between ligands and receptors.

With respect to claim 1, line 5, “reduction, or even suppression of the affinity of the interaction between the heavy chain and CD8” is vague and indefinite. It is unclear the recited language is intended as an activity limitation for a product claim, or an active step for a method claim.

With respect to claim 2, line 2, “relates to” is unclear as to how one skilled in the art to “relate.”

With respect to claim 2, line 2 “the $\alpha 3$ domain” lacks antecedent basis. Similarly, claim 3 shares the same problem as in claim 2.

With respect to claim 3, line 2, “the corresponding domain of a native heavy chain” lacks antecedent basis. Similarly, claim 4 and 5 share the same problem as in claim 3.

With respect to claim 6, line 2, "antigenic peptides" is vague and indefinite. It is unclear what "antigenic" applicant refers to. Applicant needs more specific for clarification.

With respect to claim 9, line 2, "such as" is vague and indefinite. It is unclear whether applicant intends to limit the claim with the recited feature.

With respect to claim 10, line 4, "between the modified class I MHC/peptide complexes and T lymphocyte receptors" lacks antecedent basis.

With respect to claim 10, line 7, "visualization of the lymphocyte population" is vague and indefinite. It is necessary to include necessary active steps for a method claim. It is unclear how one skilled in the art can "visualize" the lymphocyte population which are bound to the said complexes.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

4. Claims 1-4, 6-10 are rejected under 35 U.S.C. 102 (a) as anticipated by Bodinier et al. (Nature Medicine (2000) 6: 707-710)

Bodinner et al. teach a method of detecting the peptide-specific CD8 in the lymphocyte polypopulation by using the tetramers of the MHC class I with mutation (chemically modification of alanine to valine at position 245) known to reduce the interaction with CD8 (See Abstract, Figures 2-4) The mutation of alanine to valine at position 245 occurred in the $\alpha 3$ domain of HLA heavy chain where it reduces its recognition, i.e.

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affinity, to the CD8 co-receptors compared to native heavy chain binding to CD8 co-receptor. (See Abstract, page 708, left column, first paragraph) The results of the binding of the peptide-specific CD8 in the lymphocytes can be visualized by staining. (See Figure 3)

Conclusion

5. No claim is allowed.
6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jacob Cheu whose telephone number is 703-306-4086. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 703-305-3399. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4556 for regular communications and 703-308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-305-3399.

Jacob Cheu
Examiner
Art Unit 1641



July 25, 2003



LONG V. LE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

07/25/03